DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

JUL 23 1997

WARNING LETTER

Certified Mail
Return Receipt

Robert A. Forster
Managing Director
Biomet Limited
Waterton Industrial Estate
Bridgend, South Glamorgan
CF31 3YN, UNITED KINGDOM

Dear Mr. Forster:

We are writing to you because on March 14-17, 1997, an investigator, David J. Gallant, from the Food and Drug Administration (FDA) collected information that revealed a serious regulatory problem involving the product known as _____, which is made and marketed by your firm.

Under a United States Federal law, the Federal Food, Drug, and Cosmetic Act (Act), this product is considered to be a medical device because it is used to diagnose or treat a medical condition or to affect the structure or function of the body. The law requires that manufacturers of medical devices ensure that methods used in, or the facilities or controls used for the device's manufacture, packing, storage, or installation are in conformity with applicable requirements of the Act. This helps protect the public health by ensuring that medical devices are safe and effective.

In legal terms, the product is adulterated under Section 501(h) of the Act, in that the methods used in, or the facilities or controls used for manufacturing, packing, storage, or installation are not in conformance with the Good Manufacturing Practice (GMP) for Medical Devices Regulation, as specified in Title 21, Code of Federal Regulations (CFR), Part 820, as follows:

1. Failure to document planned and periodic audit results in accordance with written procedures by appropriately trained individuals not having direct responsibility for the matters being audited, as required by 21 CFR 820.20(b). This would also be a violation of the Quality System Regulation, 21 CFR 820.22. For example, there was

no documentation of internal audits of the clean room environmental control and monitoring system. Your response, dated April 15, 1997, is adequate. Procedure , Internal Quality Audits, has been updated. An audit was scheduled for the This correction will verified during the next inspection.

Failure to document specification control measures to assure that the design basis for the device and packaging is correctly translated into approved specifications, as required by 21 CFR 820.100(a)(1). This would also be a violation of the Quality System Regulation, 21 CFR 820.70(c). For example, there was no documentation of the following installation and commissioning of the clean room per referenced in Procedure

In your responses, it was stated that validation of the clean room for the has been completed. Your response is inadequate. Documentation of environmental testing, and copies of production runs for the clean room have not been provided. Adequate documentation of environmental testing and production runs for the clean room will be verified at the next inspection.

3. Failure to assure that specification changes shall be subject to controls as stringent as those applied to the original device, as required by 21 CFR 820.100(a)(2). This would also be a violation of the Quality System Regulation, 21 CFR 820.70(i). For example, no documentation of specific software changes, which were made to the production engineers on Program File was maintained and specific changes made were unknown. Your responses, dated March 26 and April 15, 1997, are adequate. Procedures were revised for modifying the

4. Failure of the critical device master record to include full and/or adequate information concerning critical components and critical component suppliers, including the complete specifications of all critical components, and the sources where they may be obtained, as required by 21 CFR 820.182(a). For example, the Device Master Record for the , does not include or reference critical components and critical component suppliers. The FDA Form 483 indicated that Biomet corrected observation 1.

5. Failure of the critical device history record to include the results of inspection checks performed, as required by 21 CFR 820.185(c). This would also be a violation of the Quality System Regulation, 21 CFR 820.80(b). For example, there was no documentation of quantified test data was not being recorded. Your responses, dated March 26 and April 15, 1997, are adequate. Receiving inspection and testing procedure has been revised, to include the number of items received, number of items inspected, and results of dimensional checks to be recorded. Correction will be verified next inspection

6. Failure to maintain a written record, including conclusions and follow-up, of the investigation of any failure of a device to meet performance specifications after the device has been released for distribution, as required by 21 CFR 820.162. This would also be a violation of the Quality System Regulation, 21 CFR 820.198(e). For example, there was no failure investigation report completed and forwarded to the complaint file, per Procedure _____. Your responses, dated March 26 and April 15, 1997, are adequate. Failure investigation reports were completed and complaints closed. A recall of the _____ has been initiated. Correction will be verified next inspection.

7. Failure to validate software programs by adequate and documented testing, when computers are used as part of an automated production or quality assurance system, as required by 21 CFR 820.61. This would also be a violation of the Quality System Regulation, 21 CFR 820.70(i). For example:

   A. There was no validation for the _____ system currently utilized to _____.

   B. The _____ which is accessed by numerous microprocessor controlled _____ has not been validated.

   Your response, dated April 15, 1997, is adequate. Validation of the _____ and the _____ has been completed. The automated system performs as intended.

8. Failure to document necessary training for performing assigned responsibilities adequately, and ensure personnel are made aware of device defects, as required by 21 CFR 820.25(a). This would also be a violation of the Quality System Regulation, 21 CFR 820.25(b)(1). For example,

   A. There was no documentation that employee was made aware of specific, improper job performance or provided corrective action training relating to Complaint _____ which revealed packaging and labeling mix-ups.

   B. There was no documentation the employee was made aware of specific, improper job performance or provided corrective action training relating to Complaint _____ which were incorrectly packaged and labeled.

   C. There was no documentation that employee was made aware of specific, improper job performance or provided corrective action training relating to Complaint _____, incorrect labeling of _____

Your responses, dated March 26 and April 15, 1997, are adequate. The employees were informed, provided corrective action training, and documented.

9. Failure to follow procedures for environmental condition monitoring, such as air pressure, to prevent contamination of the device and to provide proper conditions for each of the operations performed, as required by 21 CFR 820.46. This would also be a violation of the Quality System Regulation, 21 CFR 820.70(c). For example:

   A. Air Velocity monitoring is not being performed as required by Procedure _____

   B. _____ monitoring is not being performed as required by Procedure _____

   Your responses, dated March 26 and April 15, 1997, are adequate. procedure was revised and the clean room log sheet was modified. Correction will be verified next inspection.

This letter is not intended to be an all-inclusive list of deficiencies at your facility. It is your responsibility to ensure adherence to each requirement of the Federal Food, Drug, and Cosmetic Act and regulations. The specific violations noted in this letter and in the FDA 483 issued at the conclusion of the inspection may be symptomatic of serious underlying problems in your establishment's manufacturing and quality assurance systems. You are responsible for investigating and determining the causes of the violations identified by the FDA. If the causes are determined to be systems problems, you must promptly initiate permanent corrective actions.

We acknowledge that you have submitted to this office responses concerning our investigator's observations noted on the form FDA 483. It appears that the responses are adequate where it addresses those observations relating to software changes, Device Master Record, failure investigation reports and complaints, software validation, employee awareness of responsibilities and defective devices, and documentation of air velocity and positive air pressure gradient monitoring.

As discussed in the attached review, your responses do not adequately address those violations relating to validation of the clean room's _____ The remainder of this letter applies to those violations and the devices to which they are related.

Federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, no premarket submissions for devices to which the remaining GMP

violations are reasonably related will be cleared until the violations have been corrected. Also, no requests for Certificates For Products For Export will be approved until the violations related to the subject device have been corrected.

You should take prompt action to correct these deviations. Failure to promptly correct these deviations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties.

Please notify this office in writing within 15 working days of receipt of this letter, of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make corrections to any underlying systems problems necessary to assure that similar violations will not recur. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed. A follow-up inspection will be required, however, to assure that corrrections are adequate. Please notify this office when the facility will be ready for inspection. Until the adequacy of the corrections can be confirmed, submissions for premarket clearance will be withheld for GMP reasons. Your products will not be allowed introduction into the United States.

Your response should be sent to Linda Godfrey, Consumer Safety Office, Food and Drug Administration, 2094 Gaither Road, HFZ-306, Rockville, Maryland 20850.

You should understand that there are many FDA requirements pertaining to the manufacture and marketing of medical devices. This letter pertains only to the issue of quality system practices and does not necessarily address other obligations you have under the law. You may obtain general information about all of FDA's requirements for manufacturers of medical devices by contacting our Division of Small Manufacturers Assistance at 1 (800) 638-2041 or through the Internet at http://www.fda.gov.

If you have more specific questions about the content of this letter, please feel free to contact Linda Godfrey, Consumer Safety Officer, at (301) 594-4695, extension 143 or FAX (301) 594-4636.

Sincerely yours,

Lillian J. Gill
Director
Office of Compliance
Center for Devices and
Radiological Health

cc: Biomet Inc
Warsaw, Indiana

Review and draft: LGodfrey: 5/19/97
Revised: LGodfrey & JLazaroff: 5/29/97
Edit/Revised: JLazaroff: 6/2/97
Edit/Revised: MHoban: 6/3/97
Edit/Revised: JEisele: 6/18/97
Edit/Revised: CNelson: 6/30/97
Supv'r Concurrence: MHoban: 6/29/97
GMP Review: MCNelson: 6/30/97
Revised: LGodfrey: 7/3/97
Revised: LSpears: 7/10/97
Revised: GRodriguez: 7/21/97
Received for typing: 5/19/97
Retyped: 5/29/97
Retyped: 6/2/97
Retyped: 6/4/97
Retyped: 6/19/97
Retyped: 7/2/97
Retyped: 7/3/97 (per Louis Kaufman e-mail, guidance on GMP/QS Regulation Wording)
Retyped: 7/17/97
Retyped: 7/21/97
OC track #69173

cc:
Biomet Inc., Warsaw, Indiana
HFA-224
HFC-120
HFC-135 (DBrowning/ITOB)
HFC-230
HFC-240 (COMSTAT) (Firm is an unacceptable supplier; Remain on Auto. Det.)
HFI-35 (purged/FOI)
HFR-SW200 (DEN-DO DIB; investigator David J. Gallant)
HFR-SW140 (Compliance)
HFZ-300
HFZ-305 (PC File)
HFZ-306 (WMiller)
HFZ-343 (DOEIII firm file; chron. file)
HFZ-306 (LGodfrey; chron. file)

CFN: 9611167

Last Date of Inspection: 3/17/97
DO or ORA Endorsement: 4/21/97
ITOB Endorsement: 4/24/97
OCS Receipt date: 5/7/97
Compliance Status: W.L. remain on auto det: firm unacceptable supplier.